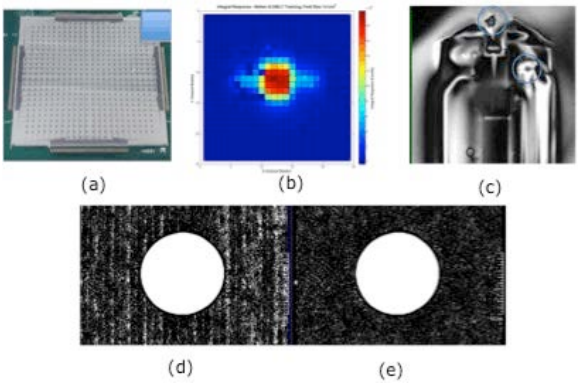

Figure 1: (a) M512 array, (b) M512 dosimetry acquisition of 1x1cm^2 field, (c) Passive M512 MR imaged at 3T, blue circles indicate fiducials (d) MR image of water phantom imaged without dosimeter noise suppression, (e) MR image of water phantom imaged with dosimeter noise suppression.

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Plerixafor Improves Local Control and Reduces Metastases in Cervical Cancer Treated with Radiotherapy and Chemotherapy

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Purpose: There is an important need to improve the effectiveness of radio-chemotherapy (RTCT) for cervical cancer. These tumors recruit myeloid cells from the bone marrow via the CXCL12/CXCR4 pathway, which in turn influence vascular function and radiotherapy response. The objective of this study was to explore combined treatment with Plerixafor (a CXCL12/CXCR4 inhibitor) and standard RTCT on primary tumor control and the development of metastases, using orthotopic primary xenografts derived directly from patients with cervical cancer.
Materials/Methods: Two primary cervix xenografts (OCICx13 and OCICx20) were grown in the cervices of immune deficient mice. These tumor models have been shown to mirror the clinical and biological behavior of cervical cancer in patients. To simulate clinical treatment, image-guided radiotherapy (30 Gy in 15 daily fractions) and concurrent weekly cisplatin (4 mg/kg) were administered, with or without Plerixafor (5 mg/kg/day). The primary endpoints were tumor growth delay, the frequency of lymph node metastases and animal survival. Chemokine expression and neutrophil recruitment were evaluated by immunohistochemistry. Acute gut toxicity was assessed using the crypt cell assay. Blood and normal organs were examined for late toxicity.
Results: The combination of RTCT and Plerixafor produced substantial tumor growth delay, reduced metastases and improved survival compared to standard RTCT alone in patient-derived xenograft models. There was a reduction in chemokine signaling (CXCL12/CXCR4) and myeloid cell infiltration (GCSF, CD11b) with combination treatment compared to RTCT alone. There was no effect of Plerixafor on acute GI toxicity, nor were there changes in blood counts or organ morphology to indicate increased late hematological or normal tissue toxicity.
Conclusion: This preclinical study demonstrates that the addition of Plerixafor to standard RTCT for cervical cancer improves local tumor control and reduced metastases with no increase in toxicity. Plerixafor is commercially available for other indications, which will facilitate translation of these findings to phase I/II clinical studies.

Keywords: Cervical cancer, radiotherapy, Plerixafor, CXCL12, myeloid cells

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Optimizing prostate cancer irradiation: from technology to fractionation

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Curative 3D standard external beam radiotherapy (EBRT) for prostate cancer has been able to improve disease control with dose escalation during the last 15 years though against the token of significant toxicity. Exploring changes in fractionation, doses-distribution optimization with modulated RT, and reducing CTV-PTV safety margins due to off- or on-line imaging before or during irradiation, may be alternatives worth to be implemented in order to reach the highest possible toxicity-free cure rates.
Accurate imaging helping to better define the irradiation target/s (e.g., multiparametric MRI, PET-CT/MRI, SPECT); modulated EBRT optimizing the dose distribution; and image guided RT (e.g., kV imaging, CBCT, fiducial markers, transponders, endorectal balloons, recto-prostatic spacers) controlling for patient repositioning and organ motion are presently available allowing the implementation of high precision treatment techniques.
Biomathematical modeling has helped to better understand the very special dose-response relationships of EBRT on prostate cancer concerning fractionation sensitivity (low α/β value), overall treatment time (tumor cell repopulation kinetics), and fraction delivery time (potential biological effective dose modifier). All these factors are rather suggestive that prostate cancer patients, especially those with low- or intermediate-risk disease, can be better treated with "more" dose/fraction, "less" number of fractions, and a "shorter" time protraction and delivery time per fraction. Two opposed modalities conceived to deliver large doses in few fractions are either stereotactic body RT (SBRT) or high-dose rate brachytherapy (HDR-BT) given alone or as a boost. The latter procedure may be limited by dose inhomogeneities and geographical misses. Even a small underdosage of the target or a heterogeneous dose-rate delivery may have a negative influence on outcome. This seems to be especially determinant for tumors with very low α/β values as it is the case for prostate cancer. Thus, SBRT may be theoretically more advantageous because the radiobiological reliability of a homogeneous dose distribution compared to HDR-BT, besides being less invasive and probably less costly.

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Evaluation of the DNA damage induced by 60 MeV proton irradiation by cytogenetic and molecular methods

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Proton radiotherapy provides a promising and emerging treatment approach for cancer patients. However, understanding of the differences in terms of DNA damage and cell proliferation post-proton irradiation is relatively poor. The purpose of this study was to evaluate DNA damage induced by proton beams using various cytogenetic and molecular methods.